

Study	Study duration (months)	Type, duration and intensity of the exercise	Exercise supervision quality	Adverse effects	Drop – out rates
Bacchi et al. 2012 [31]	4	<p><b>AET</b> (training duration: 3x60min = 180 min/wk): (1) type: cardiovascular training equipment; (2) intensity: 60-65% of reserve heart rate</p> <p><b>RT</b> (training duration: 3x60min = 180 min/wk): (1) type: 9 different exercises (involving the major muscle groups, alternating lower body, upper body, and core exercises) on weight machines and free weights; (2) intensity: 3 sets of 10 repetitions of each exercise progressing from 30–50% to 70–80% of 1 RM</p>	direct supervision (fitness center)	<p><b>AET</b>: 1 event Back pain ; 9 mild asymptomatic hypoglycemic events</p> <p><b>RT</b>: 3 events Back pain ; 1 event elbow tendonitis ; 8 mild asymptomatic hypoglycemic events</p>	<p>AET: 5%</p> <p>RT: 5%</p>
Balducci et al. 2010 [17]	12	<p><b>AET</b> (training duration: 2x60min = 120 min/wk): (1) type: treadmill; (2) intensity: 70-80% of VO<sub>2</sub> max;</p> <p><b>CT</b> (training duration: 2x60min = 120min/wk)  <b>AET</b>: (1) type: treadmill; (2) intensity: 70-80% of VO<sub>2</sub> max; (3) training duration: 2 x 40 min per week (80 min/week) + <b>RT</b>: (1) type: 4 resistance exercises (thrust movement on the transverse plane, e.g chest press or equivalent; traction movement on the frontal plane, e.g lateral pull down or equivalent; squat movement, e.g leg press or equivalent and trunk flexion for the abdominals) + 3 stretching positions. (2) Intensity: 2x20 min per week (40min/week) at 80% 1RM</p>	direct supervision (n.d)	<p>No episodes of severe hypoglycemia requiring assistance</p> <p>no adverse effects reported</p>	<p>AET: 9%</p> <p>RT: 9%</p>
Church et al. 2010 [32]	9	<p><b>AET</b> (training duration: 3x50min = 150 min/wk): (1) type: treadmill; (2) intensity: 50-80% of VO<sub>2</sub>max ; (3) aerobic dose 12 kcal/kg BW/week</p> <p><b>RT</b> (training duration: 3x50min = 150 min/wk): (1) type: upper body exercises (bench press, seated row, shoulder press, and pull down), leg exercises (leg press, extension, and flexion), abdominal crunches and back extensions; (2) intensity: 3 x week; 2 sets of 4 upper body exercises, 3 sets of 3 leg exercises, 2 sets of abdominal crunches and back extensions (each set consisted of 10 to 12 repetitions)</p> <p><b>CT</b> (training duration: 3x50min = 150 min/wk): <b>AET</b>: (1) type: treadmill; (2) intensity: 50-80% of VO<sub>2</sub>max ; (3) aerobic dose 12 kcal/kg BW/week + <b>RT</b>: (1) type: upper body exercises (bench press, seated row, shoulder press, and pull down), leg exercises (leg press, extension, and flexion), abdominal crunches and back extensions; (2) intensity: 2 x week; 1 sets of 4 upper body exercises, 1 set of 3 leg exercises, 1 set of abdominal crunches and back extensions (each set consisted of 10 to 12 repetitions)</p>	direct supervision (n.d)	<p><b>AET</b> (6 events)  <b>RT</b> (8 events)  <b>CT</b> (4 events)</p> <p>Events were: diverticulitis, emergency hysterectomy, lung cancer, 5x cardiovascular disease events, blood clot, and others (all unrelated to intervention).</p> <p>No serious adverse event occurred during exercise training; 1x was considered associated with exercise.</p>	<p>AET: 4%</p> <p>RT: 7%</p> <p>CT: 7%</p>
Cuff et al. 2003 [33]	4	<p><b>AET</b> (training duration: 2x75min = 225 min/wk): (1) type: treadmills, stationary bicycles, recumbent steppers, elliptical trainers, rowing machines; (2) intensity: 60-75% VO<sub>2</sub> max</p> <p><b>CT</b> (training duration: 3x75min = 225 min/wk): <b>AET</b>: (1) type: treadmills, stationary bicycles, recumbent steppers, elliptical trainers, rowing machines; (2) intensity: 60-75% VO<sub>2</sub> max 60-75% VO<sub>2</sub>max + <b>RT</b>: (1) type: 5 exercises (leg press, leg curl, hip extension, chest press, and latissimus pull down); (2) intensity: 3x week, 2 sets of 12 repetitions</p>	direct supervision (training classes)	no adverse effects reported	n.d

Gram et al 2010 [19]	4	<p><b>AET</b> (training duration: 2x45min = 90 min/wk in the first 2 months ; 1x45min = 45min/wk): (1) type: nordic walking ; (2) intensity: walking of at least moderate intensity &gt; 40% VO<sub>2 max</sub></p> <p><b>CT</b> (training duration: 2x45min = 90 min/wk in the first 2 months ; 1x45min = 45min/wk): AET : (1) type: ergometer cycles, rowing machines, step machines; (2) intensity: workload of at least moderate intensity &gt; 40% VO<sub>2 max</sub> + RT : (1) type: 5 exercises (chest, leg, upper back, knee extension, flexion); (2) intensity: indirect measurement “rate of perceived exertion” was used as the minimum intensity (cp. Borg Scale 13-14)</p>	direct supervision (physiotherapist)	14 events (chronic osteoarthritis, chronic low back pain, traffic accident, infections) all unrelated to intervention	AET: 5% CT: 5%
Jorge et al. 2011 [15] de Oliveira et al. 2012 [20]	3	<p><b>AET</b> (training duration: 3x60min = 180 min/wk): (1) type: cycling; (2) intensity: at heart rate corresponding to lactate threshold</p> <p><b>RT</b> (training duration: 3x60min = 180 min/wk): (1) type: a 7-exercise circuit (leg press, bench press, lat pull down, seated rowing, shoulder press, abdominal curls, and knee curls); (2) intensity: 2 sets of 10 repetitions at 50% of 1 RM in the first 2 weeks, with a 2-min rest between the circuit lap; then 4 sets of 8 to 12 repetitions at loadings constantly corrected so that all sets were sustained until exhaustion</p> <p><b>CT</b> (training duration: 3x60min = 180 min/wk): same intensity and half the volume of AET and RT</p>	direct supervision (university exercise investigation Unit, certified instructor)	Blood glucose levels were assessed if first symptoms of hypoglycemia occurred ; subjects were set to rest for 15 min. and given a 15-g carbohydrate snack  no adverse effects reported	AET: 10% RT: 10% CT: 10%
Kwon et al. 2011 [34] Ku et al. 2010 [35]	3	<p><b>AET</b> (training duration: 5x60min=300 min/wk): (1) type: walking; (2) intensity: 3.6-5.2 MET</p> <p><b>RT</b> (training duration: 3x60min=180 min/wk): (1) type: elastic resistance band exercise with 10 different motions (biceps curl, triceps extension, upright row, shoulder chest press, trunk side bending, seated row, leg press, hip flexion, leg flexion and leg extension); (2) intensity: 3 sets of 15-20 repetitions of each motion at 40-50% of maximal exercise capacity</p>	partial supervision (hospital gymnasium, at home)	no adverse effects reported	n.d
Kadoglou et al 2012 [36]	6	<p><b>AET</b> (training duration: 4x60min=240 min/wk): (1) type: 10-min warm-up, 45 min of aerobic exercises, such as walking or running on a treadmill, cycling or calisthenics, and 5-min cool down; (2) intensity: 60-75% of max heart rate</p> <p><b>RT</b> (training duration: 4x60min=240 min/wk): (1) type: 8 different exercises (leg press, knee extension, knee flexion, chest press, lat pull down, overhead press, biceps curl, triceps extension); (2) intensity: 2-3 sets of 8-10 repetitions of each exercise at 60-80% of 1 RM. The duration of each session gradually progressed over 4 weeks, where after it was maintained at 60 min for the remainder of the study.</p> <p><b>CT</b> (training duration: 4x60min=240 min/wk): same intensity and half the volume of AET and RT</p>	direct supervision (exercise trainer, fitness center)	no adverse effects reported	AET: 8% RT: 4% CT: 0%

Lambers et al. 2008 [18]	3	<p><b>AET</b> (training duration: 3x60min/wk = 180 min/wk): (1) type: treadmill walking, cycling, stepper ; (2) intensity: 60-85% of max heart rate</p> <p><b>CT</b> (training duration: 3x60min/wk = 180 min/wk)  <b>AET:</b> (1) type: treadmill walking, cycling, stepper; (2) intensity: 60-85% of max heart rate +  <b>RT:</b> stretching of the main muscle groups (10 minutes), circuit training (50 minutes): walking or jogging (10 minutes), elbow flexion and extension (10 minutes), cycling (10 minutes), knee flexion and extension (10 minutes), stepping (10 minutes), cooling down (general relaxation and stretching of the trained muscle groups); (2) intensity: 60% -85% of 1 RM, three sets of 10-15 repetitions. Between two sets a resting period of 60 seconds was allowed.</p>	direct supervision (physiotherapist)	Mild adverse events occurred 2 events of training-induced hypoglycaemia	AET: 5% CT: 10%
Moe et al. 2011 [37]	3	<p><b>AET</b> (training duration: 3x45min/wk = 135 min/wk): (1) type: cycle ergometer; (2) intensity: preparatory exercise in the first week, then exercised continuously for 45 min at 75% of their <math>VO_{2max}</math> on 2 days per week, and intermittently in five 2-min bouts at 85% <math>VO_{2max}</math> separated by 3 min of exercise at 50% <math>VO_{2max}</math> on a further day per week</p> <p><b>RT</b> (training duration: 3x45min/wk = 135 min/wk): (1) type: a brisk 5-min walk on a treadmill, followed by 5 resistance training machines: leg press, chest press, horizontal row, leg extension, and leg curl; (2) intensity: 3 sets of 8 repetitions on each machine with a resistance corresponding to 60% of baseline 1-(in kilograms), increasing in steps suited to the individual (usually 2.5 kilograms)</p>	direct supervision (n.d)	<p><b>AET:</b> no events of adverse effects</p> <p><b>RT:</b> 6 events musculoskeletal discomfort no further adverse effects reported</p>	n.d
Ng et al. 2010 [38]	2	<p><b>AET</b> (training duration: 2-3x50min/wk = 100-150 min/wk): (1) type: treadmill, stationary upright bicycle, stationary recumbent bicycle, cross trainer; (2) intensity: 65% progressing to 70% predicted heart rate</p> <p><b>RT</b> (training duration: 2-3x50min/wk = 100-150 min/wk): (1) type: 9 resistive exercises using machines and free weights (seated leg press, straight leg raise, hamstrings curl machine, biceps curls, triceps curls, lateral raises, front raises, hip abduction, hip extension); (2) intensity: 3 sets of 10 repetitions for each exercise at 65% progressing to 70% of 1 RM</p>	direct supervision (physiotherapists, hospital gymnasium)	no adverse effects reported	AET: 20% RT: 17%
Sigal et al. 2007 [16]	6	<p><b>AET</b> (training duration: 2-3x15-45min/wk = 30 -135 min/wk): (1) type: cycle or treadmill; (2)intensity: 60% progressing to 75% max heart rate</p> <p><b>RT</b> (training duration: 2-3x15-45min/wk = 30 -135 min/wk): (1) type: 7 exercises (Abdominal crunches, Seated row, Seated biceps curls, Supine bench press, Leg press, Shoulder press, Leg extension) on weight machines; (2) intensity: 2~3 sets of each exercise at the maximum weight that could be lifted 7 to 9 times</p> <p><b>CT</b> (training duration: n.d): full AET programme + full RT programme</p>	direct supervision (personal trainers, community-based exercise facility)	<p><b>AET:</b> 4 severe adverse events (worsening osteoarthritis ; 2 persons), angina (1 person), 1 newly diagnosed spinal stenosis. 4 reported mild hypoglycemia</p> <p><b>RT:</b> no severe adverse events; 4 subjects reported mild hypoglycemia.</p> <p><b>CT:</b> no severe adverse events, 2 subjects reported mild hypoglycemia.</p> <p>Adverse events occurred in 38% of the subjects ; musculoskeletal injury or discomfort requiring modification of the exercise (26%</p>	AET: 20% RT: 11% CT: 13%

				of the subjects) No episode of hypoglycemia severe enough to require assistance.	
Sukala et al. 2012 [39]	4	<p><b>AET</b> (training duration: 3x40-60min/wk = 120-180min/wk): (1) type: cycle ergometer; (2) intensity: progressed from 65 to 85% of heart rate reserve during the first 2 weeks and maintained thereafter</p> <p><b>RT</b> (training duration: 3x40-60min/wk = 120-180min/wk): (1) type: 8 major exercises (seated leg press, knee extension, knee flexion, chest press, lat pull-down, overhead press, biceps curl, and triceps extension) on weight machines; (2) intensity: 2-3 sets of 6-8 repetitions of each exercise to neural fatigue, with 1 min of rest between sets and exercises; loads increased by 5% when participants could perform 10 repetitions</p>	direct supervision (personal trainers, health and fitness facility)	One subject experienced syncope during practice  no further adverse effects reported	AET: 31%  RT: 31%
Yavari et al. 2012 [40]	12	<p><b>AET</b> (training duration: 3x 20-60min/wk = 60-120min/wk): (1) type: treadmill, elliptical or bicycle ergometers; (2) intensity: progressed from 60 to 75% of max heart rate</p> <p><b>RT</b> (training duration: 2-3 times per week): (1) type: 10 machine based exercises for upper and lower body (bench press, seated row, shoulder press, chest press, lateral pull-down, abdominal crunches, leg press, leg extension, triceps pushdown and seated bicep curls); (2) intensity: progressed from 1-2 sets during the first month to 3 sets of 8-10 repetitions of each exercise (with a 90- 120 s rest between sets) thereafter, at 75-80% 1 RM (for weeks 1 and 2: 60% of 1 RM)</p> <p><b>CT</b> (training duration: 3 times per week): AET (1) type: treadmill, elliptical or bicycle ergometers; (2) intensity: progressed from 60 to 75% of max heart rate; (3) volume: 20-30 min + RT: (1) type: 8 machine based exercises for upper and lower body (bench press, seated row, shoulder press, chest press, lateral pull-down, abdominal crunches, leg press, leg extension, triceps pushdown and seated bicep curls); (2) intensity: 2 sets of 8 of 10 exercises with 8-10 repetitions</p>	direct supervision (professional trainers)	2 subjects had repeated hypoglycaemia in the first month  no further adverse effects reported	19 %

ESM Table 1: Detailed description of the exercise programmes

AET, aerobic endurance training; CT, combined training (RT and AET); MET, metabolic equivalents; n.d, no data; RT, resistance training;  $VO_{2max}$ , maximal oxygen uptake; wk, week RM, repetition maximum; 6MWT, six-minute walk test